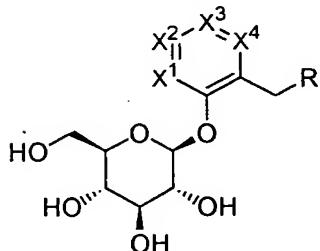


CLAIMS

1. A nitrogen-containing heterocyclic derivative represented by the general formula:



5

[wherein X^1 represents N or CR^1 ;

X^2 represents N or CR^2 ;

X^3 represents N or CR^3 ;

X^4 represents N or CR^4 ;

10 and with the proviso that one or two of X^1 , X^2 , X^3 and X^4 represent N;

R represents a C₃₋₈ cycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (A), a C₆₋₁₀ aryl group which may have the same or different 1 to 3 groups selected from the following substituent group (B),

15 a C₂₋₉ heterocycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (A), or a C₁₋₉ heteroaryl group which may have the same or different 1 to 3 groups selected from the following substituent group (B);

20 R¹ to R⁴ are the same or different, independently represents a hydrogen atom or a group selected from the following substituent group (D);

substituent group (A) consists of a halogen atom, a nitro group, a cyano group, an oxo group, -G¹, -OG², -SG², -N(G²)₂, -C(=O)G², -C(=O)OG², -C(=O)N(G²)₂, -S(=O)₂G², -S(=O)₂OG², -S(=O)₂N(G²)₂, -S(=O)G¹, -OC(=O)G¹, -OC(=O)N(G²)₂, -NHC(=O)G², -OS(=O)₂G¹.

-NHS(=O)₂G¹ and -C(=O)NHS(=O)₂G¹;

substituent group (B) consists of a halogen atom, a nitro group, a cyano group, -G¹, -OG², -SG², -N(G²)₂, -G³OG⁴, -G³N(G⁴)₂, -C(=O)G², -C(=O)OG², -C(=O)N(G²)₂, -S(=O)₂G², -S(=O)₂OG², -S(=O)₂N(G²)₂.

5 -S(=O)G¹, -OC(=O)G¹, -OC(=O)N(G²)₂, -NHC(=O)G², -OS(=O)₂G¹, -NHS(=O)₂G¹ and -C(=O)NHS(=O)₂G¹

(in the substituent group (A) and/or (B), G¹ represents a C₁₋₆ alkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkenyl

10 group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkynyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₃₋₈ cycloalkyl group which may have the same or different 1 to 3 groups selected from

15 the following substituent group (C), a C₆₋₁₀ aryl group which may have the same or different 1 to 3 groups selected from the following substituent group (D), a C₂₋₉ heterocycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₁₋₉ heteroaryl group which may have the same or different 1 to 3 groups selected from the following substituent group (D);

20 G² represents a hydrogen atom, a C₁₋₆ alkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkenyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkynyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₃₋₈ cycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₆₋₁₀ aryl group which may have the

same or different 1 to 3 groups selected from the following substituent group (D), a C₂₋₉ heterocycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (D), a C₁₋₉ heteroaryl group which may have 5 the same or different 1 to 3 groups selected from the following substituent group (D), and with the proviso that G² are the same or different when there are more than one G² in the substituents; G³ represents a C₁₋₆ alkyl group;

G⁴ represents a C₁₋₆ alkyl group which may have the same or 10 different 1 to 3 groups selected from the following substituent group (C), and with the proviso that G⁴ are the same or different when there are more than one G⁴ in the substituents; substituent group (C) consists of a halogen atom, a nitro group, a cyano group, an oxo group, -G⁵, -OG⁶, -SG⁶, -N(G⁶)₂, -C(=O)G⁶, 15 -C(=O)OG⁶, -C(=O)N(G⁶)₂, -S(=O)₂G⁶, -S(=O)₂OG⁶, -S(=O)₂N(G⁶)₂, -S(=O)G⁵, -OC(=O)G⁵, -OC(=O)N(G⁶)₂, -NHC(=O)G⁶, -OS(=O)₂G⁵, -NHS(=O)₂G⁵ and -C(=O)NHS(=O)₂G⁵;

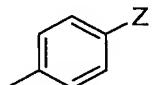
substituent group (D) consists of a halogen atom, a nitro group, a cyano group, -G⁵, -OG⁶, -SG⁶, -N(G⁶)₂, -C(=O)G⁶, -C(=O)OG⁶, 20 -C(=O)N(G⁶)₂, -S(=O)₂G⁶, -S(=O)₂OG⁶, -S(=O)₂N(G⁶)₂, -S(=O)G⁵, -OC(=O)G⁵, -OC(=O)N(G⁶)₂, -NHC(=O)G⁶, -OS(=O)₂G⁵, -NHS(=O)₂G⁵ and -C(=O)NHS(=O)₂G⁵

(in the substituent group (C) and/or (D), G⁵ represents a C₁₋₆ alkyl group, a HO-C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ 25 alkynyl group, a C₃₋₈ cycloalkyl group, a C₆₋₁₀ aryl group, a C₂₋₉ heterocycloalkyl group or a C₁₋₉ heteroaryl group; G⁶ represents a hydrogen atom, a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₃₋₈ cycloalkyl group, a C₆₋₁₀ 30 aryl group, a C₂₋₉ heterocycloalkyl group or a C₁₋₉ heteroaryl group, and with the proviso that G⁶ are the same or different

when there are more than one G⁶ in the substituents))

and with the proviso that when X¹ and X³ independently represent N or CH;

X² represents N or CR² (with the proviso that R² represents a 5 hydrogen atom, a halogen atom, a C₁₋₆ alkyl group, a C₃₋₈ cycloalkyl group, -O-C₁₋₆ alkyl, an amino group, -NH-C₂₋₇ acyl, -NH-C₁₋₆ alkyl or -N(C₁₋₆ alkyl)₂); and
when X⁴ represents N or CR⁴ (with the proviso that R⁴ represents a hydrogen atom or a C₁₋₆ alkyl group), R represents the 10 above-defined group except for the following substituent:



(wherein Z represents a hydrogen atom, a halogen atom, a C₁₋₆ alkyl group which may have a substituent selected from the following substituent group (α), -O-C₁₋₆ alkyl which may have

15 a substituent selected from the following substituent group (β), -S-C₁₋₆ alkyl which may have a substituent selected from the following substituent group (β) or a C₃₋₈ cycloalkyl group; substituent group (α) consists of a halogen atom, a hydroxy group and -O-C₁₋₆ alkyl; and

20 substituent group (β) consists of a hydroxy group and -O-C₁₋₆ alkyl)] or a pharmaceutically acceptable salt thereof, or a prodrug thereof.

2. A nitrogen-containing heterocyclic derivative as claimed in claim 1 wherein R represents a phenyl group which may have 25 the same or different 1 to 3 groups selected from the following substituent group (B), or a pharmaceutically acceptable salt thereof, or a prodrug thereof.

Substituent group (B) consists of a halogen atom, a nitro group,

a cyano group, $-G^1$, $-OG^2$, $-SG^2$, $-N(G^2)_2$, $-G^3OG^4$, $-G^3N(G^4)_2$, $-C(=O)G^2$,
 $-C(=O)OG^2$, $-C(=O)N(G^2)_2$, $-S(=O)_2G^2$, $-S(=O)_2OG^2$, $-S(=O)_2N(G^2)_2$,
 $-S(=O)G^1$, $-OC(=O)G^1$, $-OC(=O)N(G^2)_2$, $-NHC(=O)G^2$, $-OS(=O)_2G^1$,
 $-NHS(=O)_2G^1$ and $-C(=O)NHS(=O)_2G^1$

- 5 (in the substituent group (B), G^1 represents a C₁₋₆ alkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkenyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkynyl group which may
- 10 have the same or different 1 to 3 groups selected from the following substituent group (C), a C₃₋₈ cycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₆₋₁₀ aryl group which may have the same or different 1 to 3 groups selected from the following
- 15 substituent group (D), a C₂₋₉ heterocycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₁₋₉ heteroaryl group which may have the same or different 1 to 3 groups selected from the following substituent group (D);
- 20 G^2 represents a hydrogen atom, a C₁₋₆ alkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkenyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₂₋₆ alkynyl group which may have the
- 25 same or different 1 to 3 groups selected from the following substituent group (C), a C₃₋₈ cycloalkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), a C₆₋₁₀ aryl group which may have the same or different 1 to 3 groups selected from the following
- 30 substituent group (D), a C₂₋₉ heterocycloalkyl group which may

have the same or different 1 to 3 groups selected from the following substituent group (D), a C₁₋₉ heteroaryl group which may have the same or different 1 to 3 groups selected from the following substituent group (D), and with the proviso that G² are the same or different when there are more than one G² in the substituents;

5 G³ represents a C₁₋₆ alkyl group;

G⁴ represents a C₁₋₆ alkyl group which may have the same or different 1 to 3 groups selected from the following substituent group (C), and with the proviso that G⁴ are the same or different

10 when there are more than one G⁴ in the substituents;

substituent group (C) consists of a halogen atom, a nitro group, a cyano group, an oxo group, -G⁵, -OG⁶, -SG⁶, -N(G⁶)₂, -C(=O)G⁶, -C(=O)OG⁶, -C(=O)N(G⁶)₂, -S(=O)₂G⁶, -S(=O)₂OG⁶, -S(=O)₂N(G⁶)₂,

15 -S(=O)G⁵, -OC(=O)G⁵, -OC(=O)N(G⁶)₂, -NHC(=O)G⁶, -OS(=O)₂G⁵, -NHS(=O)₂G⁵ and -C(=O)NHS(=O)₂G⁵; and

substituent group (D) consists of a halogen atom, a nitro group, a cyano group, -G⁵, -OG⁶, -SG⁶, -N(G⁶)₂, -C(=O)G⁶, -C(=O)OG⁶, -C(=O)N(G⁶)₂, -S(=O)₂G⁶, -S(=O)₂OG⁶, -S(=O)₂N(G⁶)₂, -S(=O)G⁵, -OC(=O)G⁵, -OC(=O)N(G⁶)₂, -NHC(=O)G⁶, -OS(=O)₂G⁵, -NHS(=O)₂G⁵ and

20 -C(=O)NHS(=O)₂G⁵

(in the substituent group (C) and/or (D), G⁵ represents a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₃₋₈ cycloalkyl group, a C₆₋₁₀ aryl group, a C₂₋₉ heterocycloalkyl group or a C₁₋₉ heteroaryl group; and

25 G⁶ represents a hydrogen atom, a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₃₋₈ cycloalkyl group, a C₆₋₁₀ aryl group, a C₂₋₉ heterocycloalkyl group or a C₁₋₉ heteroaryl group, and with the proviso that G⁶ are the same or different when there are more than one G⁶ in the substituents)).

30 3. A pharmaceutical composition comprising as an active

ingredient a nitrogen-containing heterocyclic derivative as claimed in claim 1 or 2, or a pharmaceutically acceptable salt thereof, or a prodrug thereof.

4. A pharmaceutical composition as claimed in claim 3 wherein
5 the composition is a human SGLT2 inhibitor.

5. A pharmaceutical composition as claimed in claim 4 wherein the composition is an agent for the prevention or treatment of a disease associated with hyperglycemia.

6. A pharmaceutical composition as claimed in claim 5 wherein
10 the disease associated with hyperglycemia is selected from the group consisting of diabetes, diabetic complications, obesity, hyperinsulinemia, glucose metabolism disorders, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, lipid metabolism disorders, atherosclerosis, hypertension, congestive heart
15 failure, edema, hyperuricemia and gout.

7. A pharmaceutical composition as claimed in claim 6 wherein the disease associated with hyperglycemia is diabetes.

8. A pharmaceutical composition as claimed in claim 6 wherein
20 the disease associated with hyperglycemia is diabetic complications.

9. A pharmaceutical composition as claimed in claim 6 wherein the disease associated with hyperglycemia is obesity.

10. A method for the prevention or treatment of a disease
associated with hyperglycemia, which comprises administering
25 an effective amount of a nitrogen-containing heterocyclic derivative as claimed in claim 1 or 2, or a pharmaceutically acceptable salt thereof, or a prodrug thereof.

11. A use of a nitrogen-containing heterocyclic derivative as claimed in claim 1 or 2, or a pharmaceutically acceptable
30 salt thereof, or a prodrug thereof for the manufacture of a

pharmaceutical composition for the prevention or treatment of a disease associated with hyperglycemia.

12. A pharmaceutical combination which comprises (A) a nitrogen-containing heterocyclic derivative as claimed in claim
5 1 or 2, or a pharmaceutically acceptable salt thereof, or a prodrug thereof, and (B) at least one member selected from the group consisting of an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer, insulin or an insulin analogue, a glucagon receptor antagonist,
10 an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor, a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-1B inhibitor, a glycogen phosphorylase inhibitor, a glucose-6-phosphatase inhibitor, a fructose-bisphosphatase inhibitor, a pyruvate dehydrogenase
15 inhibitor, a hepatic gluconeogenesis inhibitor, D-chiroinsitol, a glycogen synthase kinase-3 inhibitor, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1 agonist, amylin, an amylin analogue, an amylin agonist, an aldose reductase inhibitor, an advanced glycation endproducts
20 formation inhibitor, a protein kinase C inhibitor, a γ -aminobutyric acid receptor antagonist, a sodium channel antagonist, a transcript factor NF- κ B inhibitor, a lipid peroxidase inhibitor, an N-acetylated- α -linked-acid-dipeptidase inhibitor, insulin-like growth factor-I,
25 platelet-derived growth factor, a platelet-derived growth factor analogue, epidermal growth factor, nerve growth factor, a carnitine derivative, uridine, 5-hydroxy-1-methylhydantoin, EGB-761, bimoclomol, sulodexide, Y-128, a hydroxymethyl-glutaryl coenzyme A reductase inhibitor, a fibracacid derivative,
30 a β_3 -adrenoceptor agonist, an acyl-coenzyme A: cholesterol

acyltransferase inhibitor, probcol, a thyroid hormone receptor agonist, a cholesterol absorption inhibitor, a lipase inhibitor, a microsomal triglyceride transfer protein inhibitor, a lipoxygenase inhibitor, a carnitine palmitoyl-transferase 5 inhibitor, a squalene synthase inhibitor, a low-density lipoprotein receptor enhancer, a nicotinic acid derivative, a bile acid sequestrant, a sodium/bile acid cotransporter inhibitor, a cholesterol ester transfer protein inhibitor, an appetite suppressant, an angiotensin-converting enzyme 10 inhibitor, a neutral endopeptidase inhibitor, an angiotensin II receptor antagonist, an endothelin-converting enzyme inhibitor, an endothelin receptor antagonist, a diuretic agent, a calcium antagonist, a vasodilating antihypertensive agent, a sympathetic blocking agent, a centrally acting 15 antihypertensive agent, an α_2 -adrenoceptor agonist, an antiplatelets agent, a uric acid synthesis inhibitor, a uricosuric agent and a urinary alkalinizer.

13. A pharmaceutical combination as claimed in claim 12 for the prevention or treatment of a disease associated with 20 hyperglycemia.

14. A pharmaceutical combination as claimed in claim 13 wherein a component (B) is at least one member selected from the group consisting of an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer, 25 insulin or an insulin analogue, a glucagon receptor antagonist, an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor, a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-1B inhibitor, a glycogen phosphorylase inhibitor, a glucose-6-phosphatase inhibitor, a fructose- 30 bisphosphatase inhibitor, a pyruvate dehydrogenase inhibitor,

a hepatic gluconeogenesis inhibitor, D-chiroinsitol, a glycogen synthase kinase-3 inhibitor, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1 agonist, amylin, an amylin analogue, an amylin agonist and an appetite suppressant, and the disease associated with hyperglycemia is diabetes.

15. A pharmaceutical combination as claimed in claim 14 wherein a component (B) is at least one member selected from the group consisting of an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer, insulin or an insulin analogue, a glucagon receptor antagonist, an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor, a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-1B inhibitor, a glycogen phosphorylase inhibitor, a glucose-6-phosphatase inhibitor, a fructose-bisphosphatase inhibitor, a pyruvate dehydrogenase inhibitor, a hepatic gluconeogenesis inhibitor, D-chiroinsitol, a glycogen synthase kinase-3 inhibitor, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1 agonist, amylin, an amylin analogue and an amylin agonist.

16. A pharmaceutical combination as claimed in claim 15 wherein a component (B) is at least one member selected from the group consisting of an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer and insulin or an insulin analogue.

17. A pharmaceutical combination as claimed in claim 13 wherein a component (B) is at least one member selected from the group consisting of an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer, insulin or an insulin analogue, a glucagon receptor antagonist,

an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor, a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-1B inhibitor, a glycogen phosphorylase inhibitor, a glucose-6-phosphatase inhibitor, a fructose-5 bisphosphatase inhibitor, a pyruvate dehydrogenase inhibitor, a hepatic gluconeogenesis inhibitor, D-chiroinsitol, glycogen synthase kinase-3 inhibitors, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1 agonist, amylin, an amylin analogue, an amylin agonist, an aldose reductase inhibitor, an advanced glycation endproducts formation inhibitor, a protein kinase C inhibitor, a γ -aminobutyric acid antagonist, a sodium channel antagonist, a transcript factor NF- κ B inhibitor, a lipid peroxidase inhibitor, an N-acetylated- α -linked-acid-dipeptidase inhibitor, insulin-like growth factor-I, platelet-derived growth factor, a platelet derived growth factor analogue, epidermal growth factor, nerve growth factor, a carnitine derivative, uridine, 5-hydroxy-1-methylhydantoin, EGB-761, bimoclomol, sulodexide, Y-128, an angiotensin-converting enzyme inhibitor, a neutral endopeptidase inhibitor, an angiotensin II receptor antagonist, an endothelin-converting enzyme inhibitor, an endothelin receptor antagonist and a diuretic agent, and the disease associated with hyperglycemia is diabetic complications.

18. A pharmaceutical combination as claimed in claim 17 wherein
25 a component (B) is at least one member selected from the group consisting of an aldose reductase inhibitor, an angiotensin-converting enzyme inhibitor, a neutral endopeptidase inhibitor and an angiotensin II receptor antagonist.

19. A pharmaceutical combination as claimed in claim 13 wherein
30 a component (B) is at least one member selected from the group

- consisting of an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer, an insulin analogue, a glucagon receptor antagonist, an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor,
- 5 a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-1B inhibitor, a glycogen phosphorylase inhibitor, a glucose-6-phosphatase inhibitor, a fructose-bisphosphatase inhibitor, a pyruvate dehydrogenase inhibitor, a hepatic gluconeogenesis inhibitor, D-chiroinsitol, a glycogen synthase
- 10 kinase-3 inhibitor, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1 agonist, amylin, an amylin analogue, an amylin agonist, a β_3 -adrenoceptor agonist and an appetite suppressant, and the disease associated with hyperglycemia is obesity.
- 15 20. A pharmaceutical combination as claimed in claim 19 wherein a component (B) is at least one member selected from the group consisting of a β_3 -adrenoceptor agonist and an appetite suppressant.
21. A pharmaceutical combination as claimed in claim 20 wherein the appetite suppressant is a drug selected from the group consisting of a monoamine reuptake inhibitor, a serotonin reuptake inhibitor, a serotonin releasing stimulant, a serotonin agonist, a noradrenaline reuptake inhibitor, a noradrenaline releasing stimulant, an α_1 -adrenoceptor agonist, a
- 25 β_2 -adrenoceptor agonist, a dopamine agonist, a cannabinoid receptor antagonist, a γ -aminobutyric acid receptor antagonist, a H₃-histamine antagonist, L-histidine, leptin, a leptin analogue, a leptin receptor agonist, a melanocortin receptor agonist, α -melanocyte stimulating hormone, cocaine-and
- 30 amphetamine-regulated transcript, mahogany protein, an

enterostatin agonist, calcitonin, calcitonin-gene-related peptide, bombesin, a cholecystokinin agonist, corticotropin-releasing hormone, a corticotropin-releasing hormone analogue, a corticotropin-releasing hormone agonist, urocortin,
5 somatostatin, a somatostatin analogue, a somatostatin receptor agonist, pituitary adenylate cyclase-activating peptide, brain-derived neurotrophic factor, ciliary neurotrophic factor, thyrotropin-releasing hormone, neuropeptid Y antagonist, an opioid peptide antagonist, a
10 galanin antagonist, a melanin-concentrating hormone receptor antagonist, an agouti-related protein inhibitor and an orexin receptor antagonist.

22. A method for the prevention or treatment of a disease associated with hyperglycemia, which comprises administering
15 an effective amount of (A) a nitrogen-containing heterocyclic derivative as claimed in claim 1 or 2, or a pharmaceutically acceptable salt thereof, or a prodrug thereof, in combination with (B) at least one member selected from the group consisting of an insulin sensitivity enhancer, a glucose absorption
20 inhibitor, a biguanide, an insulin secretion enhancer, insulin or an insulin analogue, a glucagon receptor antagonist, an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor, a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-1B inhibitor, a glycogen phosphorylase
25 inhibitor, a glucose-6-phosphatase inhibitor, a fructose-bisphosphatase inhibitor, a pyruvate dehydrogenase inhibitor, a hepatic gluconeogenesis inhibitor, D-chiroinsitol, a glycogen synthase kinase-3 inhibitor, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1
30 agonist, amylin, an amylin analogue, an amylin agonist, an aldose

reductase inhibitor, an advanced glycation endproducts formation inhibitor, a protein kinase C inhibitor, a γ -aminobutyric acid receptor antagonist, a sodium channel antagonist, a transcript factor NF- κ B inhibitor, a lipid

5 peroxidase inhibitor, an *N*-acetylated- α -linked-acid-dipeptidase inhibitor, insulin-like growth factor-I, platelet-derived growth factor, a platelet-derived growth factor analogue, epidermal growth factor, nerve growth factor, a carnitine derivative, uridine, 5-hydroxy-1-methylhydantoin,

10 EGB-761, bimoclomol, sulodexide, Y-128, a hydroxymethyl-glutaryl coenzyme A reductase inhibitor, a fibracacid derivative, a β_3 -adrenoceptor agonist, an acyl-coenzyme A: cholesterol acyltransferase inhibitor, probcol, a thyroid hormone receptor agonist, a cholesterol absorption inhibitor, a lipase inhibitor,

15 a microsomal triglyceride transfer protein inhibitor, a lipoxygenase inhibitor, a carnitine palmitoyl-transferase inhibitor, a squalene synthase inhibitor, a low-density lipoprotein receptor enhancer, a nicotinic acid derivative, a bile acid sequestrant, a sodium/bile acid cotransporter

20 inhibitor, a cholesterol ester transfer protein inhibitor, an appetite suppressant, an angiotensin-converting enzyme inhibitor, a neutral endopeptidase inhibitor, an angiotensin II receptor antagonist, an endothelin-converting enzyme inhibitor, an endothelin receptor antagonist, a diuretic agent,

25 a calcium antagonist, a vasodilating antihypertensive agent, a sympathetic blocking agent, a centrally acting antihypertensive agent, an α_2 -adrenoceptor agonist, an antiplatelets agent, a uric acid synthesis inhibitor, a uricosuric agent and a urinary alkalinizer.

30 23. A use of (A) a nitrogen-containing heterocyclic derivative

as claimed in claim 1 or 2, or a pharmaceutically acceptable salt thereof, or a prodrug thereof, and (B) at least one member selected from the group consisting of an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer, insulin or an insulin analogue, a glucagon receptor antagonist, an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor, a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-1B inhibitor, a glycogen phosphorylase inhibitor, a glucose-6-phosphatase inhibitor, a fructose-bisphosphatase inhibitor, a pyruvate dehydrogenase inhibitor, a hepatic gluconeogenesis inhibitor, D-chiroinsitol, a glycogen synthase kinase-3 inhibitor, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1 agonist, amylin, an amylin analogue, an amylin agonist, an aldose reductase inhibitor, an advanced glycation endproducts formation inhibitor, a protein kinase C inhibitor, a γ -aminobutyric acid receptor antagonist, a sodium channel antagonist, a transcript factor NF- κ B inhibitor, a lipid peroxidase inhibitor, an *N*-acetylated- α -linked-acid-
dipeptidase inhibitor, insulin-like growth factor-I, platelet-derived growth factor, a platelet-derived growth factor analogue, epidermal growth factor, nerve growth factor, a carnitine derivative, uridine, 5-hydroxy-1-methylhydantoin, EGB-761, bimoclomol, sulodexide, Y-128, a hydroxymethyl-glutaryl coenzyme A reductase inhibitor, a fibric acid derivative, a β_3 -adrenoceptor agonist, an acyl-coenzyme A: cholesterol acyltransferase inhibitor, probcol, a thyroid hormone receptor agonist, a cholesterol absorption inhibitor, a lipase inhibitor, a microsomal triglyceride transfer protein inhibitor, a lipoxygenase inhibitor, a carnitine palmitoyl-

transferase inhibitor, a squalene synthase inhibitor, a low-density lipoprotein receptor enhancer, a nicotinic acid derivative, a bile acid sequestrant, a sodium/bile acid cotransporter inhibitor, a cholesterol ester transfer protein
5 inhibitor, an appetite suppressant, an angiotensin-converting enzyme inhibitor, a neutral endopeptidase inhibitor, an angiotensin II receptor antagonist, an endothelin-converting enzyme inhibitor, an endothelin receptor antagonist, a diuretic agent, a calcium antagonist, a vasodilating antihypertensive
10 agent, a sympathetic blocking agent, a centrally acting antihypertensive agent, an α_2 -adrenoceptor agonist, an antiplatelets agent, a uric acid synthesis inhibitor, a uricosuric agent and a urinary alkalinizer, for the manufacture
of a pharmaceutical composition for the prevention or treatment
15 of a disease associated with hyperglycemia.